were not utilized in these cases but this is an essential step in the diagnosis of uncertain cases. Radio-active pulmonary scans[18] and determination of arterial-alveolar carbon dioxide gradients have been utilized in the diagnosis of pulmonary embolism but these measures do not seem necessary in cases of massive embolism.

Summary

Two cases of massive pulmonary embolism occurring in postoperative patients have been presented. It is believed that emergency pulmonary embolectomy with the use of cardiopulmonary bypass prevented death in both cases.

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Primary Amyloidosis With Death Due to Progressive Hypotension

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RENAL FAILURE without significant hypertension is known as a characteristic of amyloid renal disease. Yet severe, incapacitating hypotension, progressing to become a significant contributory cause of death, has been infrequently recognized as a complication of primary systemic amyloidosis. This report is of a patient in whom that occurred. A similar case was described previously by Schneckloth and Page.[6]

Report of a Case

The patient, a 48-year-old Caucasian housewife, was put in hospital in April 1962, following sudden onset of colicky abdominal pain. The blood pressure was 110/60 mm of mercury and the pulse rate 100. Muscle guarding precluded adequate abdominal examination. Four plus proteinuria was noted. An x-ray film of the abdomen showed enlargement of the liver, with the lateral tip at the right iliac crest. There were two radiopaque densities to the right of the second lumbar interspace. An intravenous pyelogram showed equal bilateral excretion at five minutes. Partial obstruction at the right uretero-pelvic junction was seen.

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At operation a rough-surfaced, dark brown calculus 1 cm in diameter was removed. As the patient had persistent low-grade fever after operation, antibiotics were given. Motile Gram-negative bacteria and white blood cells were seen in a voided specimen of urine at the time of admission and in a catheter specimen taken at the time of retrograde pyelography.

The patient was discharged from the hospital but was readmitted two weeks later because of progressive weakness, dyspnea on exertion, orthopnea, palpitations and ankle edema. Despite the edema, she had lost about 20 pounds. Blood pressure was 90/64 mm of mercury, pulse rate 120 and respirations 36 per minute. The lungs were clear and the heart not enlarged. An x-ray film of the chest was within normal limits. An electrocardiogram showed sinus tachycardia, prolonged Q-T interval and ST-T wave abnormalities consistent with electrolyte imbalance. An intravenous pyelogram did not visualize the right collecting system. Right nephrectomy was done without complication. A tissue review and special stains made of the resected kidney showed extensive amyloid infiltration of the arterioles and glomeruli. In addition, there were foci of acute and chronic pyelonephritis. At home the patient did not improve. The albumin:globulin ratio was 1.5:2.1, serum cholesterol 424 mg per 100 ml and the protein content of 2,500 ml of urine, a 24-hour specimen, was 7.7 gm.

The patient was admitted to UCLA Hospital in July 1962. Two weeks previously she had noted some small intradermal purpura on the forearms. She reported loss of hair since the onset of illness. Examination showed chemosis of both eyes and resolving subconjunctival hemorrhage. The lymph nodes were not palpable. The lungs were clear, the heart not enlarged. Due to induration and tenderness from the previous surgical incision, the liver could not be adequately evaluated. The spleen was palpable 3 cm below the costal margin. One plus pitting edema was present to mid-tibia bilaterally. Rectal biopsy was negative for amyloid. After an eight-day course of sulfisoxazole the patient was discharged with prescription of a low salt diet, chlorothiazide and potassium chloride.

At home she had episodes of palpitation, lightheadedness, weakness, and sweating on limited ambulation. These symptoms were relieved by lying down. She was readmitted to UCLA Hospital in September 1962. Blood pressure was 85/60 mm of mercury with the patient supine and fell to 70/50 mm when she sat up; at the same time the pulse rate increased from 84 to 132 per minute. The abdomen was protuberant and the flanks bulging. The liver and spleen were easily palpable about 2 to 3 cm below the costal margins. There was three plus pitting edema to the sacrum. She was given 50 gm of albumin intravenously and 100 mg of spironolactone by mouth daily for four days. The 24-hour urine protein after the first day of this therapy was 54 gm in 2,675 ml. Subsequently, the albumin:globulin ratio was 2.0:1.7. No abnormalities were seen on a radiographic series of the small bowel. Edema diminished considerably although some ascites remained. During the next month the patient was treated vigorously at home with hydrochlorothiazide, spironolactone and intermittent mercaptomerin injections. She lost about 4 kg in weight. On 19 November 1962 she fainted while waiting in the clinic. There was no detectable blood pressure and the pulse was weak and rapid. Intravenous infusion of 25 gm of albumin brought some improvement. On suspicion of adrenal insufficiency, prednisone was started in a dose of 10 mg daily. Diuretic therapy was discontinued for one week then resumed in reduced dosage after the reaccumulation of edema fluid. A trial of mephentermine initially caused a blood pressure response to 100/70 mm of mercury with the patient supine, but no blood pressure could be obtained on standing. As hypotension became worse when the effect of the drug was expended, it was discontinued.

In January 1963, the patient was readmitted and a 100 gm protein, low-sodium diet was begun and all drugs were discontinued. With this the 24-hour urine protein excretion varied from 24.4 to 28.5 gm. Bone marrow aspirate was moderately hypocellular; stainable iron was absent. Plasma cells made up 5.25 per cent of the total. The hemoglobin content of peripheral blood was 12.6 gm per 100 ml, the hematocrit 40 per cent. By measurement with radioactive chromium the red cell volume was 1,050 ml and the plasma volume 1,640 ml. On three successive days infusions of 300 ml of plasma were given. The patient gained about one pound a day and she began to have paroxysmal nocturnal dyspnea, orthopnea and anorexia. Thoracentesis was done on the left side and 960 ml of lactescent fluid with a specific gravity of 1.006 was withdrawn but there was

rapid reaccumulation. The only position in which she was comfortable was lying in bed at a 30° angle. She became faint when sitting up and dyspneic when lying flat. At this time the blood pressure was 55/40 mm of mercury supine and the pulse 110 per minute and regular. When measured in February, the blood urea nitrogen was 30 mg, creatinine 3.2 mg and albumin:globulin 0.5:2.4.

Again the patient was returned to her home but a month later, in March 1963, she had a cough productive of yellowish sputum, low grade fever and an increase in dyspnea, orthopnea, weakness and anorexia. She was readmitted to hospital. The blood pressure was 44/30 mm of mercury supine, the pulse rate 110 and respirations 28 per minute. Anasarca and wasting were striking. The liver was now 9 cm and the spleen 4 cm below the costal margins. The total serum protein was 2.6 gm per 100 ml with 12 per cent albumin (0.3 gm per 100 ml). The 24-hour urine volume was 260 ml, the serum creatinine 7.6 mg per 100 ml and carbon dioxide 15 millimols per liter. On admission 1,300 ml of clear yellow fluid was removed from the left pleural cavity. Fluid reaccumulated within 24 hours. She became stuporous and the blood pressure was unobtainable. Six hours later she died.

Throughout the course of illness there was a neutrophilic leukocytosis and the white blood cell count ranged from 10,000 to 24,000 per cu mm. The hematocrit never fell below 30 per cent. Platelets were reported adequate on all smears. Urinalysis showed specific gravity from 1.004 to 1.032, pH from 4 to 8, 3 to 4 plus protein, and no reaction for sugar or acetone. Urine sediments contained increased numbers of white cells and less often red cells, hyaline and granular casts and bacteria. On many occasions urine cultures grew more than 100,000 bacteria per ml of various species.

Autopsy

At autopsy there were 1,700 ml of fluid in the left thoracic cavity and 900 ml on the right; the abdominal cavity contained 900 ml. Numerous pale, tan, firm lymph nodes 1 to 4 cm in diameter were seen throughout the mesentery and in the mediastinum. Gross evidence of amyloid was present in the spleen, which weighed 730 gm, and in the left kidney which weighed 200 gm. The renal vein was thin-walled and patent. The liver weighed 2,000 gm. Microscopic examination of the kidneys showed that all glomeruli contained large amyloid deposits. Foci of chronic pyelonephritis were scattered throughout the cortex. The spleen was almost entirely replaced by amyloid, while liver and lymph nodes contained a moderate amount and the adrenal glands, thyroid, tongue, heart and gastrointestinal tract were diffusely infiltrated with smaller amounts. Throughout most organs examined, including striated muscle, the walls of the arterioles and the intima of the arteries were composed of amyloid. The amyloid was characteristic, but it stained poorly with Congo red. Foci of acute purulent bronchiolitis were found. Comparison of microscopic sections of the right kidney, removed in June of 1962 with those of the left kidney, examined nine months later, showed an increase in the amount of amyloid in that time, especially in the glomeruli.

Comment

The features of this case favor the diagnosis of primary amyloidosis. These include (1) the initial presentation of four plus proteinuria and enlargement of the liver, (2) the absence of a preceding history or of postmortem findings of a chronic illness known to be associated with the production of amyloidosis, (3) the finding of extensive infiltration with amyloid in the resected kidney two months after the onset of symptoms, (4) the poor staining of the amyloid with Congo red and, (5) the widespread involvement of smaller blood vessels.

The hypotension was attributed mainly to widespread amyloid infiltration of arterioles, hypovolemia and decreased venous return. Evidence of adrenal insufficiency was lacking. Responsiveness to corticotropin (ACTH) was normal when measured in July 1962. In January 1963, 24-hour urinary 17-hydroxy and ketosteroids were within normal limits (Table 1). Urinary sodium excre-

TABLE 1.—*Results of Adrenal Function Tests**

Date of Test	Steroid Contents (normal values in parentheses) 17-Keto steroids (6 to 15 mg)	17-Ketogenic steroids (5 to 8 mg)	17-Hydroxy-steroids (2.9 to 10.3 mg)
7-18-62	7.9	17.2	.....
7-19-62†	9.7	38	.....
7-20-62†	18.2	62	.....
7-21-62†	20.1	63	.....
1-11-63	6.4	.....	6.6

*Expressed as milligrams of steroid per 24-hour urine collection.
†Following corticotropin stimulation.

tion was greatly diminished during the later stages of the disease (1 to 2 mg per 24 hours). At autopsy much of the adrenal cortex was preserved despite amyloid deposits. When clinical adrenal insufficiency occurs in association with amyloidosis, it is almost always the secondary form of the disease.[3]

Amyloid cardiomyopathy may have been a major contributing factor to the hypotension, although at no time during the course of the disease was enlargement of the heart demonstrated or murmurs heard.[5] On occasion cardiac amyloidosis may mimic constrictive pericarditis.[1,4] At autopsy the heart weighed 270 gm; the valves were flexible and without vegetation; the myocardium was substantially infiltrated with amyloid. Persistent tachycardia, even at rest, may indicate a response to hypovolemia and intact cardioaccelerator sympathetic nerves.[7] Hypovolemia was demonstrated by measurement of the radioactive chromium red cell blood volume at a time when no treatment was being given.[8] The role of amyloid infiltration of peripheral and autonomic nerves was not adequately assessed by tissue examination. Except for hypotension, symptoms and signs of neuropathy were not present.[2] Blood pressure response to mephenteramine was minimal and only in the supine position; no blood pressure could be obtained with the patient standing. This minimal blood pressure response in the absence of evidence of neuropathy suggests that amyloid infiltration of arterioles played a prominent role in bringing about hypotension.[7] The presence of rather pronounced muscle wasting and inactivity, causing impaired venous return, may have augmented the presumed low cardiac output.

Diuretic therapy was helpful in alleviating excess edema and pleural effusions, but vigorous diuretic therapy enhanced the hypotension and once caused the patient to faint. Elastic stockings on the lower extremities shifted the edema fluid to the chest and abdomen without affecting the hypotension. When infusions of albumin and plasma were given, a transient rise in blood pressure occurred. During the day or two following protein infusion, urinary protein excretion increased without much change in the serum proteins. Therefore these infusions were reserved for severe hypotensive episodes.

Uremia was mild until the terminal stage of illness, and it could probably be attributed as much to poor renal perfusion as to extensive amyloid infiltration. The serum creatinine was probably a poor index of renal failure because of the muscle wasting, yet the creatinine-to-urea ratio was in the range expected.

Summary

The clinical course and pathological findings are presented of a middle-aged woman with primary amyloidosis, nephrotic syndrome and progressive, incapacitating hypotension. The hypotension appeared to be due to widespread amyloid infiltration of arterioles, hypovolemia and decreased venous return to the heart, rather than to myocardial failure, autonomic or peripheral neuropathy or adrenal insufficiency. Uremia was attributed to poor renal perfusion in addition to amyloid deposits in the kidney. Infusions of plasma and albumin were of only transient benefit in raising the blood pressure and decreasing edema. Careful diuretic therapy was successful in controlling edema and pleural effusions, but excessive diuresis enhanced hypotension.

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Generic and Trade Names of Drugs

Sulfisoxazole—Gantrisin®
Chlorothiazide—Diuril®
Hydrochlorothiazide—Esidrix,® HydroDiuril,® Oretic®
Spironolactone—Aldactone A®
Mercaptomerin—Thiomerin®
Prednisone—Deltasone,® Deltra,® Meticorten,® Paracort®
Mephenteramine—Wyamine®

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